October 18, 2007

United States Department of Agriculture

Animal and Plant Health Inspection Service

Veterinary Services

Washington, DC 20250

VETERINARY SERVICES MEMORANDUM NO. 800.92

TO: VS Management Team
Directors, Center for Veterinary Biologics
Biologics Licensees, Permittees, and Applicants

FROM: John R. Clifford /s/John R. Clifford
Deputy Administrator

SUBJECT: Potency Reference Preparation Summaries

I. PURPOSE

The purpose of this memorandum is to provide guidance regarding formatting summary information about potency reference preparations for all inactivated products. This applies to potency references for all assay formats, including, but not limited to *in vitro* assays. The information detailed in this memorandum is not different from what is already required by the Center for Veterinary Biologics (CVB). This guidance provides a suggested format for submitting the information. Utilization of the suggested format and the attached worksheet will allow for expedited review of reference-related study submissions.

II. CANCELLATION

This memorandum cancels Veterinary Services (VS) Memorandum No. 800.92, dated May 12, 1999.

III. BACKGROUND

Per Title 9, Code of Federal Regulations, Part 113.8, all *in vitro* potency tests for relative antigen content must be conducted using unexpired immunogenic reference preparations. Veterinary Services Memorandum 800.92, issued May 12, 1999, provided clarification regarding compliance with this regulation. The CVB maintains a similar policy for all other potency assays that utilize an APHIS-approved reference preparation as a minimum standard of performance for release of production serials.

V.S. Memorandum No. 800.92, issued May 12, 1999, provided an information summary to assist the CVB in tracking the status of approved reference preparations. This revised memo updates the information summary and procedures for submitting the summaries. It also provides guidance for documenting references in Outlines of Production and on Veterinary Biologics Production and Test Reports (APHIS Form 2008).

IV. GUIDELINES

A. Submission Procedures—Submission of an information summary is suggested with the following types of submissions:

1. Qualification of a new potency reference,

2. Requalification of an existing potency reference, and

3. Requests for extensions of potency reference expiration dates.

B. Information Summary - Including the following information in the information summary will allow for expedited review of reference-related study submissions. To ensure consistent formatting, a suggested summary template is provided in Appendix 1. This template is also available in a fillable pdf version on the CVB website (www.aphis.usda.gov/vs/cvb), and is posted with this memorandum.

1. Establishment Number

2. Information regarding the current potency reference submission

a. Submission date

b. Unique identifier for report

c. Primary Product Code associated with the submission

d. Purpose of report (qualify new reference, requalify existing reference, request extension of dating)

e. If the purpose of the report is to qualify a new reference, indicate the identity of the reference being replaced.

f. If the purpose of the report is to qualify or requalify a reference, indicate the date the qualification/requalification study was initiated.

3. Information regarding the identity and nature of the potency reference

a. Identification/lot number

b. Storage temperature (degrees Celsius)

c. Type of reference (master reference, working reference, or both)

d. Composition of reference

(1) Matched product: completed product that matches the product being tested, or

(2) Other completed product: product formulated like the product being tested (e.g., adjuvant type and composition) but differing in antigenic fractions (e.g., a monovalent reference used to test multi-valent product), or

(3) Non-adjuvanted microbial harvest: raw microbial culture, without further processing, or

(4) Purified antigen: Non-adjuvanted preparation processed from microbial harvest. May have differing degrees of purity, or

(5) Other: Please describe.

e. Assay protocol in which the reference is used

(1) Special Outline: include identification (ID) of Special Outline, or

(2) Supplemental Assay Method: include ID of method, or

(3) Other assay procedure described within Section V of Outline of Production for product being tested.

f. CVB test code; contact CVB-Policy, Evaluation, and Licensure if this code is unknown.

g. Working dilution: identify the dilution at which the reference is to be used

h. Product(s) tested with this reference: include all applicable product codes. Do NOT include codes for combination packages.

4. *Regulatory history of the reference* - if the purpose of the submission is to requalify an existing reference or to request an extension of dating, provide the following:

a. Original CVB approval date for reference

b. Current expiration date for reference

C. Documentation of References in the Outline of Production and APHIS Form 2008.

1. All firms should report the identity and expiration date of all reference preparations used for potency testing of serials on APHIS Forms 2008. This allows CVB to determine that an approved, unexpired reference preparation was used.

2. Firms should also update Outlines of Production in a timely manner when new references are approved for use.

Appendix 1: **POTENCY REFERENCE SUBMISSION WORKSHEET**

Establishment	

A. CURRENT SUBMISSION			
1. Submission Date		2. Report ID	
3. Primary Product Code on Submission			
4. Purpose	_____Qualify new reference _____Requalify existing reference _____Extend dating		
5. If qualifying new reference, indicate ID of reference being replaced			

B. POTENCY REFERENCE			
1. Identification/Lot No.		2. Storage Temperature	
3. Type of Reference	_____Master _____Working _____Serves as Both		
4. Composition	_____Matched Product _____Other Completed Product _____Non-adjuvanted microbial harvest _____Purified antigen _____Other (describe)_____		
5. Protocol (select one)	____Special Outline (ID_____) _____SAM (ID____) _____Other assay described in Section V Outline		
6. CVB Test Code		7. Working Dilution	
8. Additional products tested with this reference—other than code listed in part A.3 (Do not include combination packages.)			

C. HISTORY (if requalifying a reference or requesting extension of dating)	
1. Original reference approval date	
2. Current expiration date	

D. CVB USE ONLY	
1. Submission approved	_____Yes _____No
2. Approval date	
3. Assigned expiration date	
4. Comments	